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Variant: NM_002055.5(GFAP):c.235C>T (p.Arg79Cys)

Version: 1.0

CA217166

16171 (ClinVar)

Gene: GFAP (HGNC:2670)
Condition: Alexander disease (MONDO:0008752)
Inheritance Mode: Autosomal dominant inheritance
UUID: e30b7538-e38d-4403-93f8-1a260b126222
Approved on: 2026/8/18
Published on: 2026/8/18

HGVS expressions

NM_002055.5:c.235C>T
NM_002055.5(GFAP):c.235C>T (p.Arg79Cys)
NC_000017.11:g.44915252G>A
CM000679.2:g.44915252G>A
NC_000017.10:g.42992620G>A
CM000679.1:g.42992620G>A
NC_000017.9:g.40348146G>A
NG_008401.1:g.5295C>T
ENST00000253408.11:c.235C>T
ENST00000435360.8:c.235C>T
ENST00000253408.10:c.235C>T
ENST00000435360.7:c.235C>T
ENST00000586793.6:c.235C>T
ENST00000588735.3:c.235C>T
ENST00000591327.2:n.248C>T
ENST00000592320.6:c.235C>T
ENST00000638281.1:c.235C>T
ENST00000639277.1:c.235C>T
ENST00000640552.1:n.249C>T
ENST00000253408.9:c.235C>T
ENST00000376990.8:c.235C>T
ENST00000435360.6:c.235C>T
ENST00000585728.5:c.181+54C>T
ENST00000586793.5:c.235C>T
ENST00000588037.1:c.235C>T
ENST00000588316.1:c.235C>T
ENST00000588735.1:c.82+153C>T
ENST00000588957.5:c.-272+565C>T
ENST00000591327.1:n.249C>T
ENST00000592320.5:c.235C>T
NM_001131019.2:c.235C>T
NM_001242376.1:c.235C>T
NM_002055.4:c.235C>T
NM_001363846.1:c.235C>T
NM_001131019.3:c.235C>T
NM_001242376.2:c.235C>T
NM_001242376.3:c.235C>T

NM_001363846.2:c.235C>T

Pathogenic

Met criteria codes 4

PS2_Very Strong | PS4 | PM1 | PS3_Very Strong

Evidence Links 0

Expert Panel

Leukodystrophy and Leukoencephalopathy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Leukodystrophy and Leukoencephalopathy VCEP

The NM_002055.5(GFAP):c.235C>T, variant in GFAP is a missense variant predicted to cause a substitution of arginine by cysteine at amino acid 79 (p.Arg79Cys). This variant has been reported in three probands who met definite diagnostic criteria for Alexander Disease (PS4_Strong; PMID:15732097) and identified as a de novo occurrence with confirmed parental relationships in two individuals who met definite diagnostic criteria for Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PS2_Very Strong; PMID: 23364391). An aggregation assay in a zebrafish model showed a significantly higher number of GFAP aggregates than wild-type GFAP indicating that this variant impacts protein function (PS3_Very Strong; PMID: 28882119). This variant resides within a region, amino acids 59 – 88, of GFAP that is defined as a region with significant missense constraint by the ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PM1). In summary, this variant meets the criteria to be classified as a pathogenic for Alexander Disease based on the ACMG/AMP criteria applied, as specified by the ClinGen Leukodystrophy and Leukoencephalopathy VCEP: PS2_Very Strong, PS3_Very Strong, PS4_Strong, PM1 (ClinGen Leukodystrophy and Leukoencephalopathy VCEP Specifications Version 1.0.0).

Met criteria codes

PS2_Very Strong	✔	This variant has been identified as a de novo occurrence with confirmed paternal relationships in two individuals who met diagnostic criteria for Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PS2_[Very Strong]; PMID: 23364391)
PS4	✔	This variant has been reported in 3 probands who met diagnostic criteria for Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PS4_[Strong]; PMID:15732097)
PM1	✔	This variant resides within a region, amino acids 59 – 88, of GFAP that is defined as a region with significant missense constraint by the ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PM1).
	✔	

PS3_Very Strong		An aggregation assay in a zebrafish model showed a significantly higher number of GFAP aggregates than wild-type GFAP indicating that this variant impacts protein function (PMID: 28882119) (PS3_[Very Strong]).

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_002055.5(GFAP):c.235C>T (p.Arg7…	Pathogenic	Alexander Disease	2026-08-18	1.0	ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0	GFAP

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